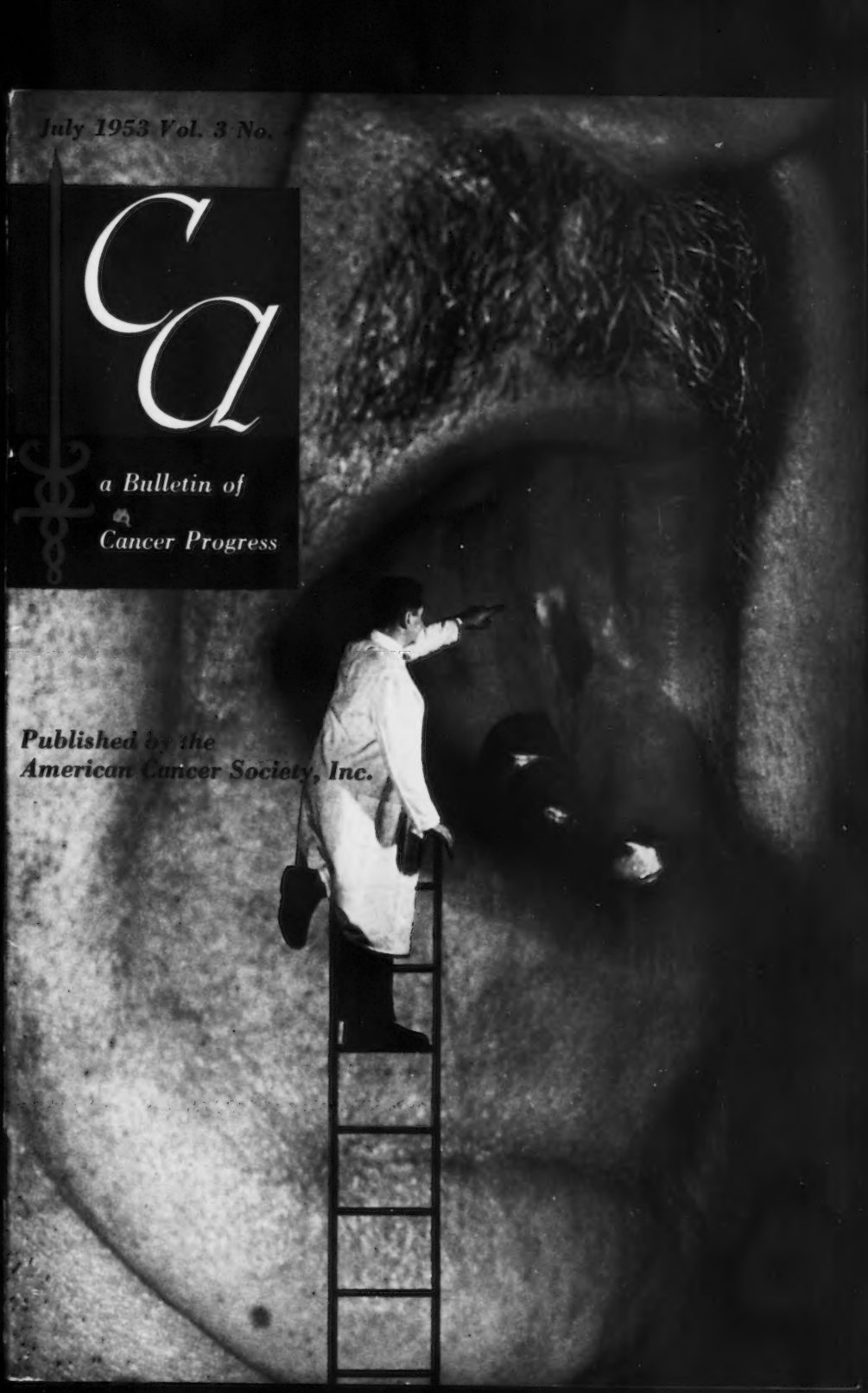
July 1953 Vol. 3 No.

Ca

a Bulletin of Cancer Progress

Published by the American Cancer Society, Inc.



The American Cancer Society and the National Cancer Institute have completed a film for doctors on the subject of the early diagnosis of cancer of the mouth. In order to have access to a large volume of suitable clinical subjects, the co-operation of a well-known cancer hospital was obtained—a hospital that admits to the house or clinic upwards of five hundred new oral-cancer patients per year. The cameras were set up, the crew stood by—and all that was needed were examples of early cancer. It took seven months to accumulate the film record, because, although an average of two new patients were examined each day, only rarely was an EARLY cancer encountered.

This is a strange state of affairs. The mouth is only slightly less accessible than the skin to examination by a physician or dentist, and most oral cancers can be seen with the help of nothing more than a light and a tongue blade. Further, so sensitive is the mouth to unaccustomed inhabitants—even tiny ones—that it is a dull patient indeed who should not himself be aware of the presence of a small tumor or ulcer. These two circumstances OUGHT to render cancer of the mouth one of the most curable forms of neoplasms.

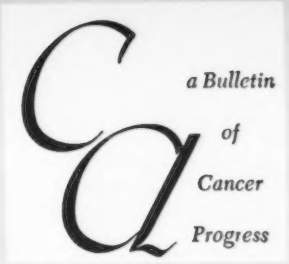
As is true for so many kinds of cancer, a small lesion, presumably early, is not a guarantee of curability. One does see minute primary tumors, unknown to the patient who presents himself to the doctor because of a bulky metastatic node in the neck. Yet it is a fact that in the mouth the correlation between the size of the lesion and the prognosis is direct enough to justify a plea for earlier diagnosis.

Cancer publicity is sometimes blamed for creating mass cancerophobia. This criticism, if it were based on fact rather than opinion, would have to be weighed against a state of affairs that is a fact, namely, that most patients with cancer of the mouth are not treated until the disease is extensive.

How to improve things? First, the public must be informed as to the significance of persistent sores, lumps, and patches in the mouth, and, if it is to be effective, doctors must endorse and, when possible, participate in such a program of public education. Second, physicians and dentists must not regard persistent (beyond two weeks) oral lesions as benign unless cancer has been excluded by biopsy. Finally, every physician and dentist should examine ALL of the oral mucous membranes of as many patients as he can persuade to say AHH.

Cover—

Lemuel Gulliver's remarkable travels have obscured his profession—that of surgeon. Evidently especially interested in tumors, he records a Brobdingnag woman "with a cancer in her breast swelled to a monstrous size, full of holes, in two or three of which I could have easily crept, and covered my whole body." And then there was "a fellow with a wen in his neck larger than five wool-packs." He writes of "a mole—as broad as a trencher, and hairs hanging from it thicker than packthreads." Gulliver's relative size made even small tumors appear enormous. Had he devoted himself to tumor diagnosis and stayed long enough, his ability to recognize small lesions would undoubtedly have lowered the cancer deaths among the Brobdingnagians substantially.



Editorial Office
American Cancer Society, Inc.
47 Beaver Street
New York 4, N. Y.

Please address all correspondence to
Charles S. Cameron, M.D., *Editor*
American Cancer Society, Inc.
47 Beaver St., New York 4, N. Y.

Published bimonthly by
AMERICAN CANCER SOCIETY, INC.
New York, N. Y.

Annual Subscription $2.50

Special bulk rate to organizations other than Divisions subscribing in quantities of 200 or more.

Keeping up

"Curative" Pancreatoduodenectomy

Patients with cancer arising in the pancreatoduodenal region generally succumb within several months following onset of symptoms. A group of three patients from the author's personal series now living eight and a half, seven, and more than five years following pancreatoduodenectomy are presented for the purpose of demonstrating that this operation is no longer an "experimental" or a palliative procedure but one that can give patients an opportunity for more than five-year survival. The cases presented three different types of cancer: carcinoma of the papilla of Vater, carcinoma of the duodenum, and carcinoma of the head of the pancreas. In two of the patients there were extensive regional lymph-node metastases. The author believes that whenever a lesion is resectable it should be removed, as this is the only chance the patient has for "cure."

Brunschwig, A.: Pancreatoduodenectomy: a "curative" operation for malignant neoplasms in the pancreatoduodenal region; report of three over-five-year survivors, Ann. Surg. 136:610-617; disc. 617-624, Oct., 1952.

Chemotherapy of Cancer

In a series of forty-two patients treated with triethylenemelamine, eighteen showed definite improvement. Patients with lymphosarcoma, Hodgkin's disease, chronic myelogenous leukemia, and chronic lymphatic leukemia showed the most dramatic improvement. Patients with fibrosarcoma, reticulum-cell sarcoma, and mycosis fungoides showed only moderate improvement. None of the patients with carcinoma benefited from the treatment. It was noted that when triethylenemelamine exerted a marked inhibition of the patient's tumor in tissue culture, it exhibited similar marked inhibition of the tumor in vivo. The drug was administered orally either in doses of 5 or 10 mg. daily in courses of one to four days or in doses of 1 mg. daily in courses of five to fifteen days. The maximum total dosage given to a single patient was 120 mg. in 168 days. When pyridoxine was administered simultaneously, toxic manifestations such as nausea and vomiting rarely occurred.

Wright, J. C.; Prigot, A.; Wright, L. T., and Arons, I.: Further observations on the use of triethylenemelamine in neoplastic diseases. A.M.A. Arch. Int. Med. 89:387-404, March, 1952.

Testicular Cancer: Diagnosis

In order to avoid delay in diagnosis, every patient with an intrascrotal swelling must be examined with the greatest care and in every case a tumor of the testis must either be discovered or definitely ruled out. Scrotal contents should also be investigated in the presence of unilateral backache or enlarged signal node in a young man. Of the tumors seen in a carefully studied series of several hundred patients, 20 per cent were erroneously diagnosed as hydroceles. Palpation should be exceedingly gentle because there may be danger of disseminating metastases by handling. The two most constant characteristics of testis tumors are hardness and heaviness. Neither incisional biopsies nor much less traumatizing aspiration biopsy should be used to obtain speci-

with Cancer

mens of testis tumors. Serological tests for syphilis should be made whenever a testis tumor is suspected, in order to eliminate the possibility of gumma of the testis. The upper regions of the body of all patients with testis swellings must be carefully examined. The earliest demonstrable lymphatic metastasis usually is situated in the abdomen on the same side as the affected testis and slightly cephalad of the umbilicus.

Excretion urograms should be taken in all patients with testis tumors. In all cases the breasts should also be examined. The Aschheim-Zondek test is especially valuable in estimating prognosis. If diagnosis is still uncertain despite careful diagnostic procedures, a patient should be referred without delay to a consultant of greater experience. Although most swellings of the testis are tumors, the minority may be gummas, infarcts, hematoceles, or torsion of the spermatic cord.

The best interests of the patient generally are served when testis lesions closely simulating tumors are promptly removed.

Dean, A. L.: Diagnosis in cancer of the testicle. New York State J. Med. 53:278-280, Feb. 1, 1953.

Carcinoma of the Stomach

A comparison was made of the 200 most recent surgical cases of carcinoma of the stomach at Charity Hospital of Louisiana with two similar series in 1941 and 1933. Gastrectomy was performed far more frequently and mortality was considerably lower in the 1952 series. Time lag was the most important factor in mortality. In terms of survival the short-term results of the palliative operation compare favorably with those of curative gastrectomy. Mortality in the third series of operations for carcinoma of the stomach, while still deplorably high, represents a considerable improvement over the two earlier series, particularly for gastrectomy. Preoperative and postoperative care was generally excellent in the latest series. In the 1952 series, eighty-two patients waited more than six months before entering the hospital and thirty-three others waited more than a year. Physicians are still treating patients symptomatically rather than investigating the cause of their symptoms. Likewise cases of carcinoma of the stomach are still mistakenly being treated as benign ulcer, although there is no positive clinical, roentgenological, or other method of differentiating gastric cancer from gastric ulcer.

Other patients in the series were treated for a wide variety of other diseases, most of which they did not have. Carcinoma of the stomach was not suspected in most of these patients. There was also an alarming trend toward a period of delay for neuropsychiatric consultation. The solution of the problem of carcinoma of the stomach obviously lies in the finding of early cases. Nothing is so valuable as a well-taken clinical history. There should be a prompter and more general resort to exploratory laparotomy in doubtful cases.

Boyce, F. F.: Carcinoma of stomach; comparison of three series of surgical cases in large general hospital. J.A.M.A. 151:15-20, Jan. 3, 1953.

a glance . . .

one-minute abstracts of the current literature on cancer . . .

Tumors of the Mouth and Upper Air Passages

Multiple myeloma, a progressive and fatal disease, is characterized by the presence of widely scattered tumors in the bone marrow. A study was made of a series of twenty-seven histologically proved plasma-cell tumors in the mouth, nose, nasopharynx, pharynx, or larynx. Eighteen of the patients were men; twenty were more than 50 years of age. According to site of origin the tumors may be grouped as follows: nasal cavity, 8; antrum, 6; sphenoidal sinus, 1; nasopharynx, 2; soft palate, 1; tonsil, 1; tongue, 1; mandible, 6; extrinsic larynx, 1.

In most of the cases the tumors were first thought to be epidermoid carcinoma and biopsy was required to establish a diagnosis. In one third of the cases the condition was actually multiple plasma-cell myeloma presenting itself first as a solitary lesion in the upper air passages.

The finding of "myeloma" cells in representative marrow punctures and the presence of a high total serum protein with a reversal of the normal albumin:globulin ratio seem to indicate the existence of the multiple form of the disease. It is believed that solitary plasmacytoma and multiple plasma-cell myeloma are in the vast majority of cases only variants of the same disease process. It is unsafe to regard any of these lesions as noncancerous. It is thought that there is no very sharp line of demarcation between localized, benign plasmacytomas on the one hand, and the malignant, fatal multiple myelomas on the other. In seven patients the plasmacytoma was confined to the soft tissues. In the remaining eleven the tumor appeared to be solitary with evidence in each case of involvement of the adjacent bone. Treatment is by surgery, radiation, or a combination of the two procedures.

Ewing, M. R., and Foote, F. W., Jr.: Plasma-cell tumors of the mouth and upper air passages. Cancer 5:499-513, May, 1952.

Radiology in Laryngeal Cancer

Radiography, particularly tomography, is of assistance in the diagnosis of carcinoma of the larynx. Biopsy if done by a skilled laryngologist is not dangerous. It is particularly useful in differentiating postirradiation changes from persistent disease or recurrence. Early lesions may be treated successfully by laryngofissure. In advanced

lesions the only feasible operation is laryngectomy. Radiotherapy by teleradium, needles, or roentgen rays is in general more successful and results in less deformity and a better functional result than surgery. Local recurrences following radiotherapy are not suitable for further irradiation. If radiotherapy failure is recognized early, surgical treatment is still possible in the majority of cases. Radiation therapy may fail because of a too-advanced lesion, subglottic extension, or the combination of pachyderma with cancer. The cases reported include forty in whom laryngectomy was performed, twenty-seven treated with radium needles, 103 receiving teleradium therapy, and thirteen treated solely by roentgen rays.

Cade, S.: The influence of radiology in the diagnosis and treatment of intrinsic carcinoma of the larynx. Mackenzie Davidson Memorial Lecture. Brit. J. Radiol. 24:582-588, Nov., 1951.

Cancer of the Tongue

An analysis is given of seventy-six consecutive cases of cancer of the tongue admitted to the New York University Hospital during the years 1935 to 1945. Treatment in general consisted of surgical removal of the tongue lesion by the knife or electrocautery in combination with block dissection of all superficial and deep cervical nodes, whether there was clinical evidence of metastasis or not. In those cases in which the tongue lesion had grown to involve the floor of the mouth, with grossly involved cervical nodes, treatment was by radical resection of the primary tumor with or without a portion of the mandible and radical homolateral neck dissection in continuity. Age of the patient in itself is not a contraindication to radical neck dissection. Cancer of the tongue, like cancer elsewhere in the body, should be considered in relation to the so-called "cancer field." It has been the policy of the present clinic to recommend bilateral complete "prophylactic" cervical node dissections for carcinoma of the tongue in all patients who have a reasonable life expectancy. Many primary tongue cancers can be treated successfully by radiation. However, much time may be wasted if the primary tumor proves in the end to be radioresistant, because surgery must then be carried out in damaged tissue with poor healing properties.

The primary lesion was treated surgically in sixty-six cases of the present series. Forty patients were submitted to node dissections. There were no deaths following prophylactic node dissection. Seven cases considered inoperable were treated by radiation in the form of roentgen rays or radium or both. Radon-needle implantation was used as treatment of choice in two cases. One patient had received palliative treatment elsewhere, was given terminal care, and died in one month. Twenty-nine patients lived at least five years without evidence of recurrence. There were four postoperative deaths and five died of intercurrent disease without evidence of cancer in less than five years. No crossed metastases were found unless the homolateral nodes were involved. Two cases were lost to follow-up.

Lyall, D., and Schetlin, C. F.: Cancer of the tongue. Ann. Surg. 135:489-496, April, 1952.

Tumors of Parotid Salivary Gland

Successful surgical removal of parotid tumors rests on two principles: (1) complete removal of the tumor and (2) avoidance of unnecessary injury (either temporary or permanent) to the seventh cranial nerve or its larger branches. The ideal surgical procedure for the majority of benign or malignant parotid tumors would be the removal of the tumor together with a portion of the parotid gland and the preservation of all or whatever branches of the nerve are not involved by the growth. Many growths of the parotid gland are incompletely removed because the surgeon fears to injure the facial nerve. In order to avoid such injury the best procedure is the routine exposure and identification of the nerve first, before proceeding with the actual removal of

the tumor. In the Head and Neck Clinic at Memorial Hospital the main nerve is approached immediately and directly just after it emerges from the stylomastoid foramen to enter the parotid gland. A description is given of the form of skin incision and the operative technique for parotid tumors with preservation of the seventh nerve.

Martin, H.: The operative removal of tumors of the parotid salivary gland. Surgery 31:670-682, May, 1952.

Roentgenotherapy in Oral Cancer

In an attempt to achieve better control of primary cancers of the mouth, the roentgen-ray tumor dose was greatly increased in conjunction with techniques designed to minimize the amount of radiation to the normal tistues. All patients were accepted for treatment, regardless of the extent of the primary lesion or of the metastases. Most of the patients were elderly. All lesions treated were proved epidermoid carcinomas. In general, cases referred for radiation were those in which there was some specific contraindication to surgical treatment, such as inaccessibility of tumor, size such as to preclude the possibility of excision, or general physical condition contraindicating operation or anesthesia. During a three-year study, fifty-five patients were treated with conventional dosage of roentgen rays, whereas sixty-three patients were given massive doses (more than 7000 r). Delivery of tumor dosages in the low therapeutic range resulted in a minimum recurrence or persistence rate of well over 50 per cent, whereas the massive tumor dose effected excellent control. Of the entire group of sixty-three patients who received massive therapy, twenty-five are still alive with no evidence of local lesion, thirteen having survived more than three years since the primary disease was treated. The only two complications encountered following massive therapy were radiation ulcer and radiation necrosis. Greater assurance of control of the primary cancer allows earlier treatment of metastatic neck nodes.

White, G., and Christensen, W. R.: Control of inoperable oral cancer with massive roentgen therapy. New England J. Med. 245:719-723, Nov. 8, 1951.

Survival Rate in Cancer of the Larynx

Results of treatment of cancer of the larynx for all patients seen at the Massachusetts Eye and Ear Infirmary between 1930 and 1945 on whom there is an accurate follow-up are as follows:

Treatment	*No. cases*	*Dead*	*5-year cure*
Irradiation	231	190	41—17.7%
Laryngofissure	54	22	32—59 %
Laryngectomy	104	43	61—58 %
Cord cancer—x-rays	13	1	12—92 %
Total	402	256	146—36.3%

The author concludes that carcinoma of the larynx is still a serious disease and that five-year results still depend on early diagnosis and prompt treatment. Cancer of the larynx still calls for a careful evaluation and individual consideration of each case. The type of treatment must be based on the pathology of the lesion, on the extent of the disease, on its duration, and on the condition of the patient.

Schall, L. A.: Symposium: Carcinoma of the larynx. IV. Cancer of the larynx; five year results. Quart. Rev. Otorhinolar. & Bronchoesoph. 10:151-154, Dec., 1951.

Credits

The five doctors in "Falcon's Eye, Girl's Hands, Lion's Heart," pages 22 and 23, January, 1953, are by Goodrich and Rush, Advertising Art Service, New York City.

The cover for March, 1953, a photograph of the two million volt x-ray machine in the Radiation Therapy Department of the Hospital for Joint Diseases is by Michael Hollander, *Photography*, New York City.

Leukoplakia

Grant E. Ward, M.D.

Leukoplakia is a white patch on the mucous membrane of a cavity lined with squamous epithelium. It is common in the mouth and is sometimes found in the vagina, on the cervix, and in the anal canal. In the mouth it may be found on the inner side of the lip, gingiva, buccal mucous membrane, palate, and the tongue. Paradoxically, it appears dry, although bathed in saliva. The surface is usually flat and broken by tiny fissures in the squamous epithelium giving a mosaic pattern. Very superficial leukoplakia, in which the epithelium is not piled up sufficiently to produce these little cracks, may appear smooth, flat, and white.

Pathogenesis

Leukoplakia is a hyperplasia of the squamous epithelium that, microscopically, appears indistinguishable from hyperkeratosis so commonly found on the skin. The squamous epithelium is hyperkeratinized and thickened. In the mouth, it does not scale off as does hyperkeratosis on the skin because it is covered constantly with saliva. This hyperkeratotic process when on the lip may take the form of leukoplakia on the mucous-membrane side and of hyperkeratosis along the vermilion border, which is exposed to air and dried. In a cross section of the lip having leukoplakia on the mucous-membrane side and hyperkeratosis on the vermilion border and skin, it would be impossible to differentiate between the two processes, leukoplakia and hyperkeratosis, were it not for the mucous glands on the inner side of the lip, indicating mucosa, and hair follicles and sebaceous glands on the skin side.

Etiology

It is generally accepted by the medical profession that leukoplakia many times is secondary to chronic trauma. In support of this view is the fact that when chronic trauma—such as tobacco, bad-fitting denture, or rough, ragged teeth—is eliminated, many of the patches of leukoplakia improve or completely disappear. Ewing, Boyd, and others attest to the fact that leukoplakia is evidence of some type of chronic irritation. Syphilis is often blamed for the origin of leukoplakia. Sturgis and Lund found clinical evidence of syphilis in 17 per cent of the cases of oral leukoplakia and in 2 per cent of cases of keratosis of the lip. The serological test for syphilis was positive in 27 per cent of the cases of oral leukoplakia and 13 per cent of the cases of keratosis of the lip. Such a high percentage of syphilis may be present in average dispensary patients, but in our private practice certainly syphilis has not played an important role in leukoplakia of the mouth, with the exception of leukoplakia located on the tongue.

Harry S. Robinson, Sr. states that in his opinion very few patients with leukoplakia, exclusive of that of the tongue, have positive serological tests for syphilis. The reverse is also true—that is, very few people with known syphilis develop leukoplakia in the mouth. J. Earle Moore avers that there is practically no relationship between leukoplakia of the buccal mucosa and syphilis. On the other hand, he is sure that a definite relationship between syphilis and leukoplakia of the tongue exists. Moore further affirms that there are not enough statistically significant data to make a positive statement as to the percentage of leukoplakia of the tongue caused by syphilis.

Leukoplakia on the tongue associated with syphilis is usually accompanied by atrophy of the papillae, par-

Baltimore, Maryland.

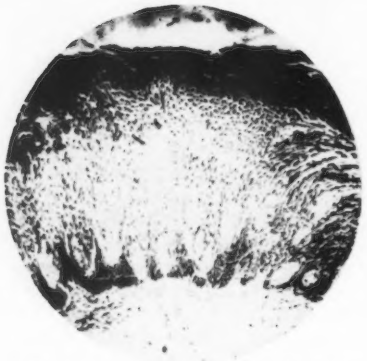


FIGURE 1. Photomicrograph of an area of leukoplakia. Note thickening of squamous mucous membrane and hyperkeratinization at the surface. There is a slight amount of inflammatory reaction beneath.

ticularly along the edges, and appears as rather thick, scattered patches and sometimes as sheets. Also, there is apt to be marked scarring of the tongue, with firm nodules between the scars, giving what I have termed "hobnail tongue."

In recent years attention has been called to the possible role of avitaminosis A and C in the etiology of leukoplakia. In support of this theory is the fact that in many patients treated with large doses of vitamins A and C (100,000 units of vitamin A and 500 mg. of vitamin C a day) there is marked improvement in the leukoplakia after a period of one, two, or three months.

On the other hand, it is not uncommon for patients with no evidence of chronic irritation or syphilis to develop leukoplakia. This observation has led to the assumption that there is an unknown underlying biological etiological factor. It should be borne in mind that leukoplakia in many instances is a precancerous lesion. Mantilla, quoted by William Boyd states that ". . . of 566 cases of leukoplakia buccalis, including the tongue, 32 per cent developed carcinoma."

The patient illustrated in Fig. 3 A, B, and C, illustrates the lack of a known etiological factor in the formation of leukoplakia and the premalignant nature of this disease. The patient was an elderly edentulous woman of 80 years who did not use tobacco and wore no denture. On her first visit there was a well-developed area of leukoplakia on the right side of the dorsum of the tongue in front of the faucial pillar. The diseased area was destroyed by electrodesiccation. The serological test for syphilis was negative. One year later, the patient came back with a typical highly differentiated carcinoma in the scar.

It should be emphasized here that not all cases of leukoplakia become malignant. The ones most prone to malignant transformation are thick, rapidly growing patches that frequently have a more or less verrucous appearance. Leukoplakia that is thin and widely scattered through the mouth and present for many years (ten, fifteen, or twenty) is less apt to develop cancer.

Clinical Behavior

In the past, leukoplakia has been classified according to its etiology—to-

FIGURE 2. Photomicrograph of leukoplakia in a more-advanced stage. Note downgrowth of rete pegs and more marked inflammatory reaction in the submucous tissue than is seen in Fig. 1. The basement membrane is still intact.

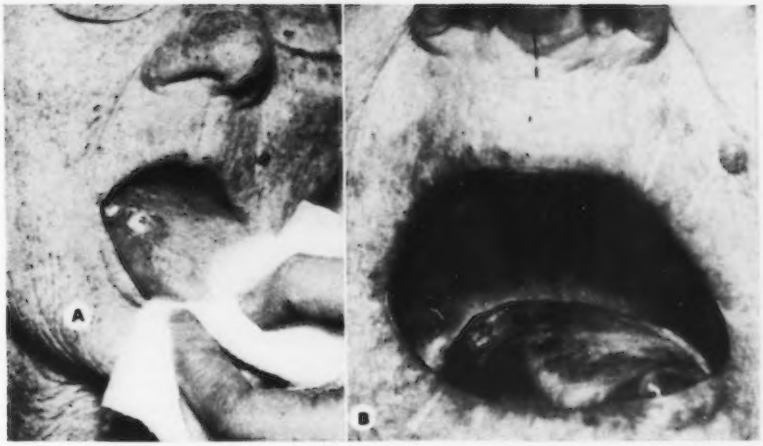


FIGURE 3. A, Leukoplakia in an 80-year-old woman, who did not use tobacco and whose serological test for syphilis was negative. It healed after electrosurgical removal. B, Squamous-cell carcinoma developing in the scar one year later.

bacco, syphilis, etc. Such a classification, however, does not include all types. From a rather long experience, Ward and Hendrick described a classification of leukoplakia that is entirely clinical.

1. This group may be called "acute leukoplakia," in that the history dates back only a few weeks or months (Fig. 5). These lesions develop rapidly, become thickened, and some of them actually ulcerate or develop papillomas. Such leukoplakias are more apt to become malignant than the second group.

2. Chronic leukoplakia may last as long as ten, fifteen, or twenty years. This type is more diffuse and much thinner in appearance, resembling a white film over the surface of the mucous membrane. On the palate, tiny red pinhead-sized lesions may be present appearing like tiny craters. In the center of these craters is a tuft of capillaries that bleed on slight trauma. One of our patients, a doctor in his 70's, could draw blood from these areas simply by sucking against the top of his mouth. He smoked a pipe with a hole in the top of the stem. The hot smoke flowed out over the palate and kept up the irritation. After changing to a pipe with a hole in the end of the stem, the bleeding stopped, but there was no appreciable change in the leukoplakia. Another patient was referred because occasionally he found blood on the top of the tongue, which he concluded came from the tongue. Examina-

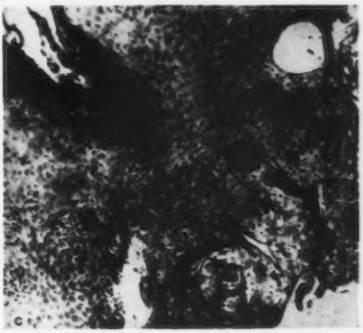


FIGURE 3. C, Photomicrograph shows typical squamous-cell carcinoma developing in leukoplakia. Note hyperkeratinization and pearly bodies.

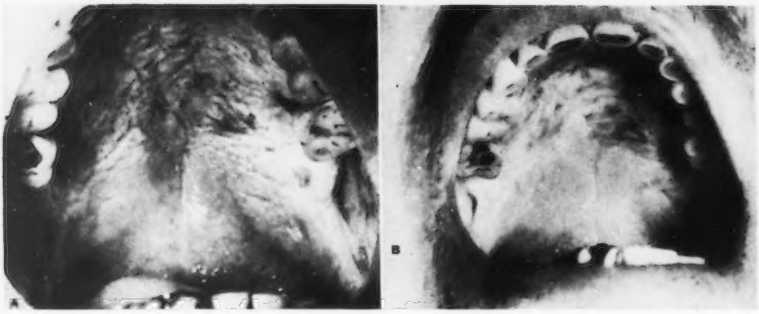


FIGURE 4. A, Acute leukoplakia involving the mucous membrane of the hard palate. Notice the thickened, piled-up squamous epithelium and tiny craterous areas, which are more frequently seen in the chronic form of leukoplakia on the palate. This patient also had squamous-cell carcinoma of the floor of the nares, Grade II, treated with irradiation about a year previously. At that time, there was no leukoplakia in the mouth. B, Marked improvement after one month's treatment with 100,000 units of vitamin A daily; treatment was continued for three months.

tion disclosed that the tongue was normal, but there was a patch of leukoplakia on the hard palate with several tiny craterous ulcers. Biopsy showed no cancer. Rarely do these long-standing leukoplakias become malignant.

FIGURE 5. Area of thickened, piled-up leukoplakia on the buccal surface just inside the angle of the mouth. This is a common site for leukoplakia. This lesion disappeared under treatment. The patient returned four years later with squamous-cell carcinoma in the same area.

3. A third intermediary group could be established as a "subacute variety." This type probably represents the early forms of the more chronic leukoplakias and stands intermediary both in duration of the disease and the stage of development between types 1 and 2, usually behaving like the latter.

Differential Diagnosis

Careful examination of the entire oral cavity and lymph nodes of the neck is necessary to make an accurate diagnosis of leukoplakia of the mouth. A serological test for syphilis is necessary to rule out this disease as an etiological factor. When the lesion contains a hard nodule, or is ulcerated or papillomatous, or fixed to underlying tissue, biopsy of an appropriate site is mandatory to rule out cancer.

There are other lesions of unknown etiology that may confuse the observer unfamiliar with leukoplakia. Lichen planus (Fig. 10) and psoriasis are among these. Psoriasis usually has a more lacelike, shiny appearance and is much more superficial than leukoplakia. Lichen planus often presents as a small pinhead- to larger-sized white

FIGURE 6. Leukoplakia on the upper right gingiva. The patient had a squamous-cell carcinoma removed from the right premolar area with electrosurgery three years previously at another hospital. This was followed by irradiation. The serological test for syphilis was positive. The patient came to the clinic this time with a small patch of leukoplakia on the lingual side of the upper right gum. The lesion disappeared following irradiation.

FIGURE 7. Chronic leukoplakia of the right buccal mucous membrane. Notice how much thinner the lesion appears than that in the acute variety shown in Fig. 4A. The mucous membrane appears dry, granular, and in the anterior portion of the lesion somewhat puckered from scar. This type is less likely to become malignant than the acute variety.

spot or may be annular or papular. Careful dermatological examination in such cases may be rewarded by revealing skin lesions of these diseases. Lloyd Ketron states that psoriasis never occurs in the mouth, and that lichen planus sometimes is present without any skin manifestations. Leukoderma is a rare intraoral lesion to be differentiated from leukoplakia. It is flat, smooth, and not fissured.

Treatment

Treatment should always begin by removing all possible types of chronic irritation, such as ill-fitting dentures, bad teeth, and excessive smoking. One of my patients who smoked sixteen cigars a day presented with a very heavy leukoplakia on practically all the mucous membrane of the mouth except the tongue. Eliminating tobacco caused marked improvement. Other methods were necessary to eradicate the disease completely—namely, high doses of vitamins A and C and, later, of roentgen-ray therapy to the buccal surfaces.

On one clinic day at Johns Hopkins Hospital two patients appeared with leukoplakial spots on corresponding areas on their tongues, opposite a ragged molar tooth. Dental care caused one lesion to heal, and the other developed cancer. These two cases illustrate the danger lurking behind many leukoplakial spots.

If the elimination of irritating factors does not permit the leukoplakia to disappear, and when a definite proof of cancer is lacking, the areas are treated in one of several ways.

Choice of Treatment. The choice of

treatment depends entirely upon the type and size of the area. Tiny superficial areas may be watched carefully for months. Any change in size or thickness demands treatment. Small superficial patches of limited extent are readily destroyed with electrodesiccation. Larger areas are controlled with roentgen-ray therapy, or radium, either in one massive dose, or broken into two or three applications. Two thousand gamma-roentgens broken into two or three applications, spaced several days to a week apart, are usually sufficient to cause second degree blistering of the mucosa, which heals in from two to four weeks leaving a good, pale, superficial scar.

Pyott et al. have described an efficient acrylic applicator with lead protection to hold the radium against the oral mucosa. With modern roentgen-ray cones, however, such a costly acrylic applicator is hardly necessary.

Unfortunately, many cases of leukoplakia are resistant to one or the other of these types of treatment. It is not uncommon to desiccate small areas lingering after irradiation or to irradiate areas residual after electrodesiccation.

During the last three years or more, we have been using large doses of vitamin A and vitamin C orally in most cases whether treated with other modalities or not. This therapy was based on the results of dermatologists in the treatment of hyperkeratoses with high doses of vitamin A. Fifty thousand units of vitamin A and 250 mg. of vitamin C are given orally twice a day. Improvement is usually not seen until after one or two months, and the therapy is carried on for at least three or four months, sometimes longer. Some patients affirm that the skin of the face becomes much softer and that they feel generally better. Such high doses of vitamin A sometimes cause epigastric distress requiring reduction in amount or, occasionally, discontinuance of it.

FIGURE 8. A, Scarred nodular tongue from tertiary syphilis. Notice the hobnail appearance caused by marked scarring between the elevations. B, Photomicrograph showing hyperplasia of the squamous epithelium and round-cell infiltration. (A and B reproduced from the Cyclopedia of Medicine, Surgery and Specialties by permission of the F. A. Davis Co.)

FIGURE 9. Syphilitic glossitis. Note whitish leukoplakia and atrophy of the papillae on both sides of the tip of the tongue.

FIGURE 10. Lichen planus of the left buccal mucous membrane. Note the small pinpoints of whitish lesion and the white streaks that differentiate this from leukoplakia.

It should be emphasized again that patches of leukoplakia that are thickened, adherent, ulcerated, papillomatous, or contain hard nodules demand biopsy of an appropriate site. The hard nodules on the edge of the ulcer or the base under the papillomatous area are such sites for biopsy.

All cases of leukoplakia require observation for months and years after treatment. Any recurrence should receive therapy. Although not all cases of leukoplakia become malignant, this disease is considered as a preneoplastic process. The rapidly growing areas of short duration apparently are the result of some as yet unknown biological reaction that, if adequate treatment is not given, leads to the development of cancer.

References

1. *Boyd, W.: Surgical Pathology, 6th ed. Philadelphia. W. B. Saunders Co. 1947.*

2. *Ewing, J.: Neoplastic Diseases; a Treatise on Tumors, 4th ed. Philadelphia. W. B. Saunders Co. 1940.*

3. *Ketron, L.: Associate Professor of Dermatology, Johns Hopkins Medical School, and Dermatologist-in-Charge of the Dermatological Clinic, Johns Hopkins Hospital. Personal communication.*

4. *Moore, J. E.: Associate Professor of Medicine, Johns Hopkins Medical School, and Physician-in-Charge, Venereal Diseases Clinic, Johns Hopkins Hospital. Personal communication.*

5. *Pyott, J. E.; Bruder, V. F. J.; Manion, W. J., and Ward, G. E.: Leaded resinous applicator for intraoral and extraoral radium therapy. Am. J. Roentgenol. 47: 613-619, 1942.*

6. *Robinson, H. S., Sr.: Professor of Dermatology and Syphilology, University of Maryland Medical School. Personal communication.*

7. *Sturgis, S. H., and Lund, C. C.: Leukoplakia buccalis and keratosis labialis. New England J. Med. 210: 996-1006, 1934.*

8. *Ward, G. E., and Hendrick, J. W.: Diagnosis and Treatment of Tumors of the Head and Neck. Baltimore. Williams & Wilkins Co. 1950.*

Wide excision of a carcinoma that formerly seemed inoperable because of local secondaries is now attempted more often because of improvements in technique and the use of antibiotics, e.g., wide excision of carcinoma of the palate or antrum was not often attempted until the advent of sulfonamides and especially penicillin.

Gavey, C. J.: The Management of the 'Hopeless' Case. London. H. K. Lewis & Co. Ltd. 1952, p. 25.

Diagnosis and Treatment of Cancer of the Extrinsic Larynx

Chevalier L. Jackson, M.D.

Much has been written about the importance of early diagnosis of hoarseness, and the marvelous results obtained by simple surgical treatment, as well as by skilfully administered radiotherapy, in the treatment of early cancers of the vocal cord. Not so much has been said about the diagnosis or treatment of cancers of the epiglottis, the aryepiglottic folds, or the pyriform sinuses, the so-called "extrinsic" areas, and I believe there are two reasons for this. In the first place, the symptoms are not so clear-cut and they do not develop until later in the growth of the tumor. In the second place, the results of treatment have been so discouraging as to make the surgeon or radiologist less eager to report results.

Symptoms

The symptoms of cancer of the extrinsic or "silent" areas of the larynx are vague discomfort in the throat—later pain; sensation of foreign body or "lump in the throat"; in the more advanced stages only, hemoptysis, hoarseness, dyspnea, and dysphagia. It is, of course, in the stages of vague discomfort and sensation of foreign body that we must strive to make the diagnosis. Emphasizing the possible significance of such symptoms will naturally bring to the doctor's office many anxious neurotic patients and will cause many apprehensive introspective individuals some sleepless nights, but, in the interest of promoting earlier diagnosis and raising the cure rate of cancer, we must ignore these objections. Of course, we should always combine with our warnings the reassurance that early diagnosis means cure.

Examination

Assuming that the patient with symptoms suggestive of extrinsic cancer of the larynx or hypopharynx has come to us, what examinations are indicated? First, of course, we must make an ordinary examination of the nose, mouth, and pharynx with a proper light and proper instruments. Then a careful examination is made with a good laryngeal mirror of proper size (No. 5 is suitable in average adult cases) and a good headlight or reflected light. If satisfactory visualization of the larynx AND PYRIFORM SINUSES is not obtained without the use of a local anesthesia, then a spray of 10 per cent cocaine or 2 per cent pontocaine should be used.

Visualization of the entire interior of the larynx, right up into the anterior commissure is necessary, and it should be remembered that motility, which is an important sign, is best determined on cordal ABduction, immediately after phonation. The cord that does not ABduct is impaired or fixed, and this is an important sign. Careful inspection of both surfaces of the epiglottis and the ventricular bands and aryepiglottic folds can be made both during quiet breathing and on phonation. Finally, the pyriform sinuses and posterior hypopharyngeal wall are carefully examined and they are best seen on phonation because this movement opens them widely and holds them open, as the arytenoids and vocal cords maintain approximation.

From the Department of Laryngology and Broncho-Esophagology, Temple University Medical School, Philadelphia, Pennsylvania.

FIGURE 1. Extrinsic lesion of larynx involving the right epiglottic fold and the right margin of the epiglottis.

Direct examination with the direct laryngoscope and the short esophagoscope may be resorted to for supplementary inspection, but generally this should be preceded by thorough fluoroscopic and roentgenographic studies. The use of an opaque mixture is necessary to outline the pyriform sinuses and to visualize the swallowing function. Ordinary lateral roentgenograms are valuable, but the addition of sectional planigraphic films greatly increases the assistance afforded by the roentgenologist in these cases. While a histopathological diagnosis should not be attempted from roentgenograms, the graphic representation of the soft-tissue masses is most helpful, when considered along with the other findings.

If the indirect laryngoscopic and roentgen-ray examinations are both negative, direct inspection can generally be postponed. If a lesion is visualized or suspected, direct examination will be the next step, except in cases of conspicuous lesions of the epiglottis or aryepiglottic folds, which can be easily biopsied by the indirect method.

Palpation of the neck is necessary in all cases, because the presence of metastatic nodes is a very important factor in planning treatment.

Differential diagnosis requires the exclusion of tuberculosis by chest roentgenograms and, of course, biopsy. The commonest cause of "lump in the throat" is anxiety and this condition is known as "globus hystericus"—but the diagnosis is justifiable only after careful examination has excluded an organic lesion.

Treatment

Formerly, lesions of the extrinsic area were considered by most surgeons "inoperable," and those who did attempt to extirpate them surgically were almost always unsuccessful. The great majority of such patients were therefore turned over to the roentgenologist for treatment. Very encouraging results were obtained in some cases, especially in tumors of the epiglottis. The pendulum has now swung, in most quarters, toward surgical treatment, however, and that means, generally, laryngectomy with extirpation of the lymph-node–bearing tissue on the affected side. Better results are being obtained than formerly by better surgical techniques, better understanding of the management of cervical metastases (which means always doing a thorough surgical extirpation of the nodes when nodes are palpable, and doing "elec-

FIGURE 2. Direct laryngoscopy, the method of examination most satisfactory for full visualization of the lesion and for biopsy. (From Jackson and Jackson: Diseases of the Nose, Throat and Ear. Philadelphia. W. B. Saunders Co. 1945.)

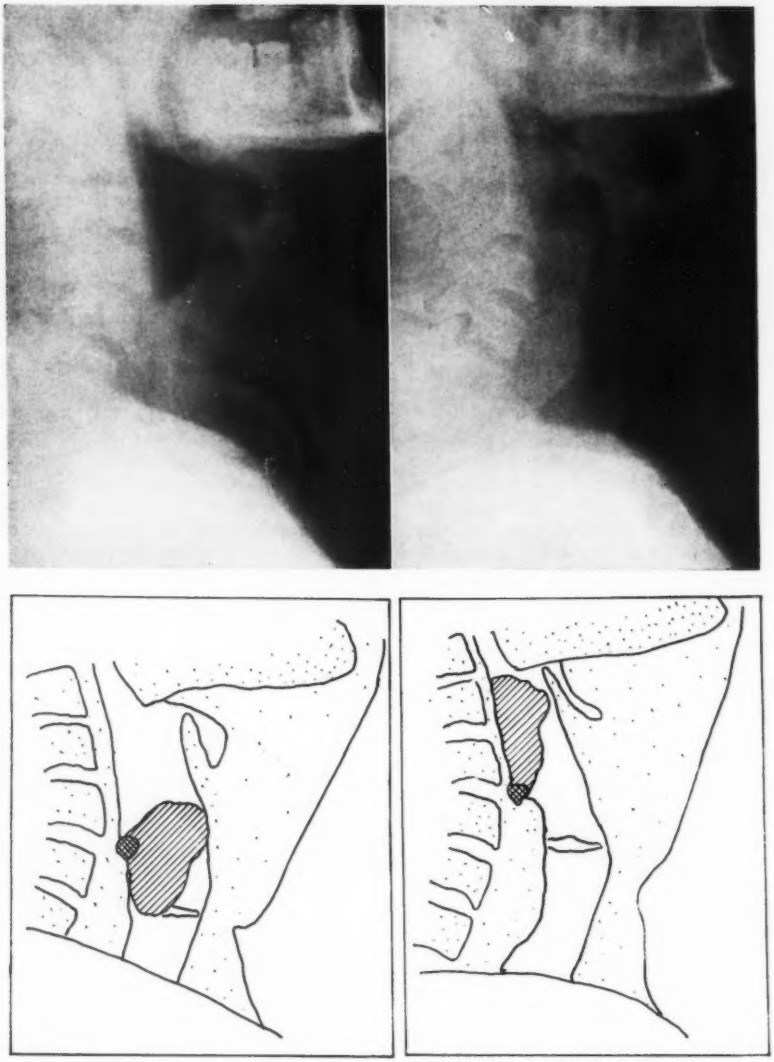


FIGURE 3. Lateral roentgenogram of the neck, showing a large pedunculated extrinsic carcinoma discovered by the roentgenologist when the patient was being studied, at the request of his internist, because of a wheeze. Note that the tumor flopped down into the supraglottic lumen on inspiration, or on leaning forward, with resultant dangerous respiratory obstruction.

FIGURE 4. Advanced carcinoma of the base of the epiglottis involving the base of the tongue.

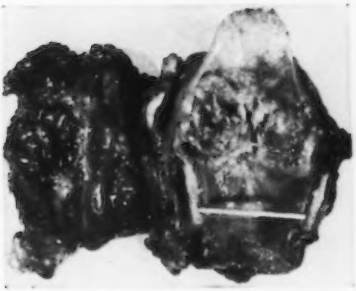


FIGURE 6. Carcinoma of the base of the epiglottis in a 55-year-old man with no palpable nodes. A laryngectomy was done, with simultaneous extirpation of the lymph-node–bearing area, but the pathologist did not find any evidence of metastasis.

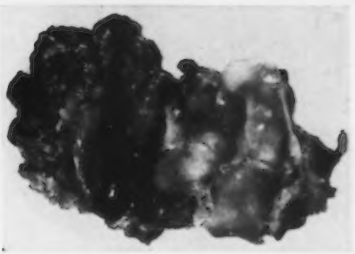


FIGURE 5. Extrinsic carcinoma involving the left side of the epiglottis and the left ventricular band in a man 56 years of age. No nodes were palpable at the time of operation, but the lymph-node–bearing area on the left side was removed in continuity with the larynx and histological study showed metastasis. Two months later a palpable node developed on the right side, and a right "neck dissection" was done.

tive" neck dissections in some cases in which palpable nodes have not yet developed), and, especially, by earlier diagnosis. By way of further encouragement it should be noted that newer surgical procedures of partial laryngectomy have been developed that now make it possible to extirpate the very early lesions of the epiglottis or of the pyriform sinus, with or without the tributary nodes, without sacrificing the whole larynx.

Conclusion

It must be stated that the day has arrived when the extrinsic lesion has "come into its own," and both the profession and the public should be educated in its proper understanding. Vague symptoms and signs referable to the throat call for careful examination, and if a lesion of the extrinsic larynx is found it should receive prompt and thorough treatment.

LESIONS OF THE ORAL CAVITY

Figure 1. Indurated ulcer of six weeks' duration: epidermoid cancer, Grade II. Likelihood of cure exceeds 80 per cent.

Figure 2. Leukoplakia: a precancerous lesion.

Figure 3. Relatively large cancer, superficially ulcerated, yet smaller than the average coming to treatment!

Figure 4. Granuloma. Soft nodular tumor indistinguishable from cancer except by biopsy.

Figure 5. Leukoplakia of the buccal mucosa associated with early cancer.

Figure 6. Cancer of the lower gum, associated with leukoplakia and invasion of bone.

Figure 7. Small carcinoma of the floor of the mouth arising at the base of the frenulum.

Figure 8. Extensive leukoplakia of the floor of the mouth.

Figure 9. Papilloma (benign) of the buccal mucosa.

Figure 10. Squamous carcinoma, Grade II, of the palate. Patient was conscious of this papillary lesion for four months but did not consult doctor until soreness developed.

Figure 11. Cancer of the buccal mucosa. The growth, more than 2 cm. in diameter, near the labial commissure, has obviously been present for several months.

The central portion is ulcerated and excavated, and the borders of the growth are elevated and covered with leukoplakia. The delay in seeking medical advice in this case was probably due to the patient's untroubled acceptance for several years of an area of leukoplakia, which only slowly increased in extent, with an imperceptible change toward malignant transformation, and finally to ulceration and excavation. There was an absence of both pain and tenderness until a few weeks before admission.

Figure 12. Cancer of the tonsil. An ulcerated indurated growth is present in the left tonsil.

Diagnosis of Early Cancer of the Mouth

Hayes Martin, M.D.

It is a universal and time-honored belief that the chance of cure in any serious disease depends upon how early the treatment can be given. It is for this reason that a doctor is expected to respond to emergency calls at any hour of the day or night. Furthermore, the average person accepts it as perfectly reasonable that an ambulance bearing a sick person must have the right of way through the thickest of traffic so that the patient may obtain treatment at the earliest possible moment. While such an attitude is entirely reasonable, nevertheless, in the case of one of the most serious diseases of all, namely, cancer, there is no clear understanding as to what constitutes an early stage and early treatment of the disease.

The average layman is of the opinion that all serious diseases are associated with either marked discomfort or disability, and therefore that a lesion or a complaint that might suggest cancer nevertheless remains in an early stage for a fairly long period, as long as the symptoms are not actually painful or disabling, and that there is little necessity to begin treatment until the symptoms do become distressing. Obviously this is not true, for all physicians and most laymen have at least known of cases of hopelessly and incurably advanced cancer in various parts of the body, in which there was no great discomfort and in which, to all external appearances, the patient enjoyed robust health.

Mouth Cancer and the Family Physician or Family Dentist

The patient with cancer usually applies first to the family physician or dentist. If, after this first application for medical advice, a correct diagnosis of cancer should be made within a few days (often in early and curable stages of the disease), the credit rightly belongs to the physician or dentist who first suspected the possibility of cancer and either properly advised or referred the patient, so that a diagnosis of cancer was promptly made.

With the present-day tendency toward specialization in all technical skills, much has been written deploring the de-emphasis of the role of the general practitioner or the family physician in the medical care of the community. For the public welfare, it must be conceded that no array of specialists, no matter how skilled, can ever replace the family doctor who, in most cases, is a general practitioner. While specialization is necessary for particular skills, nevertheless, if the average layman with the complaints and symptoms of any illness were to go directly to the so-called "specialist," he must of necessity first have made his own diagnosis in order to select the doctor. Obviously, this is neither reasonable nor practical. All sensible persons have a family doctor or a medical adviser, just as they have someone to go to for legal or financial advice (family lawyer or banker). In medicine and dentistry, no matter how much a practitioner may restrict his activities in order to develop certain narrow skills, he must willy-nilly remain the "family doctor," the "family dentist," or the "medical adviser" to a considerable number of people who will continue to consult him at least by telephone as to what to do or where to go for some particular symtom or complaint. In this sense, all members of the medical and dental professions remain FAMILY DOCTORS to a great number of their patients and even

to their acquaintances. It is not too much to expect, therefore, that all members of the medical and dental professions should be familiar, at least in a general way, with the characteristic symptoms of early cancer in all parts of the body, so that when appealed to they may give the proper counsel.

Symptoms of Cancer of the Mouth

The symptoms of early mouth cancer are seldom distressing or markedly painful. As a matter of fact, many persons with hopelessly advanced, bulky growths involving most of the tongue or palate, even with bilateral cervical metastases, may actually have suffered little pain or discomfort up to the time of admission. Medical advice in many cases is finally sought only because of the increasing disability in speech, in masticating food, or in initiating the act of swallowing. Obviously, those patients who first seek medical advice in such an advanced stage of the disease have already noted the objective symptoms for several months. Owing to the mild nature of the symptoms of early mouth cancer, early diagnoses can be made only in the cases of reasonably intelligent patients, who will consult a well-informed and astute physician or dentist while their symptoms are still mild and of short duration.

Early Symptoms. There are only four common early symptoms of mouth cancer. In the order of their frequency, they are as follows: (1) persistent localized soreness or tenderness in the mouth or throat; (2) the discovery by the patient of a painless, nontender lesion (sore or lump); (3) slight persistent difficulty or pain on swallowing; (4) a lump in the neck (cervical metastases).

Localized Pain or Tenderness. In the anterior portion of the mouth (tongue, floor of mouth, cheek), a localized soreness or pain is the most common symptom (in almost half the cases). Such a symptom is also characteristic of a number of benign or noncancerous conditions—for instance, accidentally biting the tongue, heavy smoking, taking a mouthful of too hot food, subacute tonsillitis, and so forth. Most persons have experienced such mild and transient complaints repeatedly and tend to accept them for a time without undue concern. Such localized tenderness may induce a person to examine the affected area visually and thereby lead to the discovery of the lesion itself. The reason for localized pain or tenderness in mouth cancer is that there is at least mild infection in an ulcerated growth. Such symptoms are not specific of cancer, since localized pain or tenderness is inevitable in any lesion of the mouth in which continuity of the mucous membrane is broken. As a matter of fact, most traumatic lesions caused by biting the tongue or burning with hot food are more painful than cancerous lesions. Pain or tenderness is not present on admission in almost half the malignant growths of the mouth, and NO GREATER DIAGNOSTIC ERROR CAN BE MADE THAN TO CONCLUDE THAT A SUSPICIOUS LESION IN THE MOUTH IS BENIGN RATHER THAN CANCEROUS BECAUSE OF THE ABSENCE OF PAIN OR DISCOMFORT. As a matter of fact, the contrary is more reasonable. Cancer may be painless and nontender. Traumatic and benign inflammations are always tender.

Discovery of a Painless, Nontender Lesion. The second most common initial symptom in mouth cancer is purely objective—that is, the patient states that a "lump," a "rough spot," or a "sore" was seen or felt on the lip, tongue, or somewhere in the mouth. This indicates that, by the tactile sense of the tongue, some irregularity of the surface was felt and that, in the mirror, the lesion itself was visualized. If the suspicious area is on the gum or palate, the disease is likely to be considered of dental origin and therefore the dentist will be consulted. The tactile sense of the anterior portion of the tongue is rather acute. Both during mastication and during speech, the tip of the tongue comes in contact rather generally with

the mucous membranes of all the anterior portions of the mouth. In these areas the irregularity of the mucous surface, which in many cases is early cancer, can hardly escape detection.

In the posterior portion of the mouth, for instance, in the base of the tongue, the tactile sense is not particularly acute, so that cancers in this area, in the absence of localized pain, tend to grow to a large size before discovery. For example, in cancer of the tonsil, the average size of the growth is about 4 cm. in diameter when the patient first applies for treatment. In the anterior portion of the mouth or lips, the diagnosis can be made much earlier.

Slight Persistent Pain or Difficulty on Swallowing. In cancers of the posterior portion of the oral cavity, (base of tongue, tonsil, palate, pharyngeal walls), because of the absence of acute tactile or pain sense, the most common early symptom is a slight dysphagia. There may be either slight persistent pain on swallowing, or the act of swallowing may be difficult to initiate and carry through because of actual infiltration of the musculature of the base of the tongue or tonsillar area sufficient to restrict the normal movements. In such cases, the problem is difficult. Symptoms of slight pain on swallowing or the sensation of a "lump" in the throat are common symptoms. In patients with anxiety neuroses, there is no way of differentiating the one from the other, except by an examination with a throat mirror and the exploring finger to palpate the mesopharynx and the base of the tongue. In such examinations, it is relatively easy to rule out those who do not have cancer, and to reassure the patient with a marked cancer phobia that the globus hystericus is not of serious consequence. Repeated examination and reassurances may be required in some of the more apprehensive patients.

A "Lump in the Neck." In many forms of mouth and pharynx cancer, the site of the primary lesion is relatively insensitive—for instance, the nasopharynx, the base of the tongue, the tonsil, the pharyngeal wall, the extrinsic larynx—and the growth may persist for a period of several months without producing any symptom whatever at the local site. In many of these cases, the first abnormality noted by the patient is what is usually called a "lump in the neck." Such a cervical tumor may be disregarded for a considerable time, until symptoms occur in the primary site —"sore throat" (in cases of cancer of the base of the tongue, tonsil, pharynx, or extrinsic larynx), "soreness in the mouth" (in cases of mouth cancer), deafness in one ear or diplopia (in cancer of the nasopharynx). If medical advice is sought at a time when there are both symptoms in the primary site and a "lump in the neck," there should be little difficulty in a tentative diagnosis on the first examination by a well-informed physician or dentist.

In other cases, however, the patient seeks medical advice complaining only of a "lump in the neck," and, all too frequently in these cases, the physician may conclude that the cervical tumor is the primary disorder, and he is therefore concerned only in establishing its nature or in removing the mass. The unwisdom of such a concept is proved by the fact that precocious cervical metastasis ("lump in the neck") is the first symptom in a large proportion of cancers of the mouth and pharynx. These percentages are given in Table 1. It is surely significant that, in cancer of the nasopharynx (the primary site of which is one of the most difficult of access for physical examination), a "lump in the neck" is the first symptom IN MORE THAN HALF THE CASES. Even in such readily accessible sites as the anterior floor of the mouth, such a "lump" is the first symptom in about 10 per cent of the cases. These figures should be proof to fair-minded physicians that when a patient complains only of a "lump in the neck" of reasonably short duration (excluding such obvious conditions as lipoma or thyroid adenoma of many years' duration), it is most

likely that the "lump" is metastatic (lymph-node) cancer, especially if the enlargement is asymmetric. Consequently, if the cervical mass is cancerous, then it is almost certainly metastatic from a silent primary lesion somewhere in the mouth or pharynx. The diagnostic procedure to be undertaken in such cases will be discussed under a subsequent heading.

Clinical Findings in Mouth Cancer

To objective examination, a malignant tumor of the mouth usually appears as an ulcer that is more indurated than the tissues from which it arises. The surface granulations are usually coarse in texture and have a rather healthy aspect, as opposed to the yellowish smooth appearance of an inflammatory lesion. The induration usually extends beyond the borders of the ulcer into the surrounding tissues. The borders of the lesion are usually raised and somewhat undermined. In some of the cases the ulcer is excavated, but usually the overgrowth of cancerous tissue protrudes or fungates to some extent above the level of the surrounding surface.

None of these just-mentioned findings should be taken as having any exclusive meaning. In some cases, a cancer arising in the mucous membrane of the base of the tongue, and less often in its anterior portion, may apparently not ulcerate at all from the surface, but rather invade deeply. In other cases in which cancer arises in a leukoplakial patch, there may be no detectable induration, and the malignant portion then appears as a small, flat, smooth ulcer only 2 to 3 mm. in diameter.

When the growth is both visible and palpable through the open mouth, these just-mentioned findings are fairly obvious. When, however, the growth is at the base of the tongue, the pharyngeal wall, or nasopharynx, its character may have to be established by inspection alone.

TABLE 1

Incidence of Precocious Cervical Metastasis in Head and Neck Cancer—Review of 1300 Cases, 1947–1949

Head and Neck Service—Memorial Hospital

Anatomical site of primary lesion	% cases with a cervical mass as the initial symptom
Nasopharynx	47
Tonsil	28
Base of tongue	23
Thyroid gland*	23
Extrinsic larynx	17

*In this group (23 per cent), the cervical mass was specifically not in the thyroid gland per se but rather in the lateral aspect of the neck.

Differential Diagnosis of Mouth Cancer

It can be stated without hesitancy that mouth cancer is more serious and more important to the patient than any other condition with which it might be confused. Therefore, in any suspicious lesion of the mouth, the physician or dentist should consider cancer first and should rule out such a possibility before "waiting to see what happens" or proceeding with treatment on the basis of a benign diagnosis. Actually, if a lesion of the mouth is not cancerous, it is rarely of any great clinical significance from the standpoint of danger to life. If the possibility of a malignant growth is considered at the beginning, few harmful errors in diagnosis will be made.

The benign lesions that are similar in appearance to cancer are relatively rare and include tuberculous ulcers, gumma, pyogenic granuloma, and sometimes trauma, when the patient has accidentally bitten his tongue. Gumma of the tongue has never been a common lesion and is practically never seen in these times, since the advent of antibiotics and better venereal disease control. Tuberculous ulcers of the mucous membranes (almost always in association with advanced pulmonary tuberculosis) sometimes resemble

cancer, but the differential diagnosis is readily made by biopsy. Pyogenic granuloma is also rare and sometimes cannot be differentiated except by biopsy. Accidentally biting the tongue is a history given by many patients with cancer who thereby hope to relieve their dire suspicions that they may have cancer and to justify their delay in seeking medical advise. Such histories should be disregarded if the lesion looks suspicious. Benign, thin, nonulcerated leukoplakia is readily differentiated from the thickened, fissured, partly ulcerated variety in which malignant transformation may have taken place. There are several fairly common benign neoplasms of the mouth, such as giant-cell epulis, pregnancy tumor (granuloma of the gum), fibroma of the tongue or gum, hemangioma, etc. Most of these are fairly characteristic in appearance. Papilloma so much resembles cancer that the diagnosis can only be made by biopsy, and the treatment by surgical excision is the same as for cancer.

Management by the Physician or Dentist in Cases of Suspected Mouth Cancer

If the physician or dentist is cancer-conscious, he will be alert to discover suspicious areas in the mouth or lumps in the neck of which the patient may be unaware. He will also be alert to interpret the nature of the complaint of the patient who states that there is a "rough spot," a "sore spot" in the mouth, a pain or "soreness" on swallowing, or a "lump in the neck." He should be able to decide whether or not this complaint or abnormality is sufficiently suggestive of cancer to require further investigation. In many cases the physician or dentist may be able to carry through these investigations himself, even to making a biopsy. In others, it is his responsibility to see that the patient does have the benefit of more specialized opinion if such is required. If physicians and dentists in general are cancer-conscious, few early cases of mouth cancer coming under their observation will be missed.

Biopsy. The only sure proof of cancer is a histological examination of a tissue specimen, without which any diagnosis must be only tentative. If aggressive treatment, either by surgery or radiation, is to be given, a positive biopsy must be obtained and, should such biopsy be omitted for a specific reason, then it is the responsibility of the one who treats the case should the diagnosis be in error.

Everything else being equal, the biopsy examination in the average case had best be made by the one who is to give the treatment, and, if the person with obvious cancer can be got into such hands without biopsy, then that is the best disposition. In certain cases in which the physician or dentist wishes to avoid the psychological upset that might be associated with an attempt to refer the patient elsewhere, it may be best to make a biopsy and get a histological diagnosis first. In these cases, any other method of management might only result in alarming the patient and having him "run for cover," rather than expeditiously proceeding to settle the matter.

If the physician or dentist therefore feels that the best plan would be to make an immediate biopsy, he should, after local infiltration of an anesthetic, bite out, sometimes with the aid of a scalpel, a fragment of tissue about 4 to 5 mm. in diameter from the ulcerated border of the tumor, place it immediately in 10 per cent formalin, and forward it to a competent pathologist. If the report is returned as showing cancer, the physician or dentist may then approach either the patient himself or one of the family with the convincing proof that further treatment is essential.

Summary and Conclusions

The patient with mouth or throat cancer, complaining either of local symptoms in these areas or of a "lump in the neck," will usually apply to the family doctor, to the family dentist, or to whatever medically trained person is

TABLE 2

Five-Year–Cure Rates in Mouth Cancer, 1943–1945

Head and Neck Service—Memorial Hospital

Site of primary lesion of cancer	% 5-yr.–cure rate in all cases (all comers both early and advanced)	% 5-yr.–cure rate in early and moderately advanced cases (primary lesions less than 2 cm.)
Lip	78	92
Tongue	28	49
Floor of mouth	28	50
Mucosa of cheek	27	40
Palate (hard and soft)	34	60
Gum	26	50
Tonsil	20	45

usually consulted first for directions in cases of illness. Only rarely is a so-called "specialist" or a tumor clinic consulted first. It is therefore essential that the first physician or dentist consulted be sufficiently cancer-conscious to recognize the possibility of cancer and either to proceed with the diagnostic measures or to refer the patient elsewhere, where such diagnostic procedures can be carried out.

From the standpoint of prognosis for permanent cure, the importance of early diagnosis in mouth cancer is readily demonstrated. In Table 2 is given the five-year–cure rate in all comers (early and advanced) with cancer in certain primary sites in the mouth. In the second column is given the corresponding cure rates in early or moderately advanced lesions (less than 2 cm. in diameter). In this table it is seen that the cure rate in the earlier stages is at least twice, sometimes three times, as great as in the over-all cases, including both early and advanced. Such a figure should be eloquent proof of the importance of early diagnosis, and should bring to the attention of all members of the medical and dental professions their responsibility toward the public welfare and the large part that they play in the reduction of the death rate from cancer of the mouth.

Hoarseness in Cancer of Larynx

Dr. A. J. Brizzolara (Little Rock, Ark.) states that hoarseness is the key to early diagnosis of laryngeal cancer. Any hoarseness persisting for more than two weeks, particularly in patients beyond 35 years of age, must be considered to be caused by cancer until proved otherwise. Interference with voice function brings the patient to the doctor early, since the voice is the primary means of communication. Hoarseness presents an opportunity for the physician to spot cancer of the larynx earlier than cancer can be detected elsewhere in the body. Beginning hoarseness, the first symptom, is practically simultaneous with the beginning of growth of the cancer, and, if this warning is heeded immediately, cure may be obtained.

CANCER CLINICS

A major advance in our fight against oral cancer was accomplished by the organization of the first consultative tumor board in a dental school, at the School of Dentistry, University of Southern California, in September, 1949. A further bond was created between the medical and dental professions because members of both professions are on the board, and this board is becoming an important oral diagnostic unit in Southern California. It co-operates with consultative tumor boards in hospitals and medical schools, and with private practitioners in both professions.

In order that all phases of the oral-tumor problem be covered, positions and suitable members were selected as follows (all members are heads of departments or board members): Chairman, R. L. Fowkes, D.D.S.; Pathologist, Weldon Bullock, M.D.; Tumor Consultant, George Sharp, M.D.; Oral Surgery, John Svoboda, D.D.S., and Leo Fogel, D.D.S.; Tumor Diagnosis, Cecil Collins, D.D.S., and Paul Hamilton, D.D.S.; Prosthetics, Frank Lott, D.D.S.; Oral Medicine, John W. Hazlet, D.D.S.; Secretary, Harry E. Straub, D.D.S. Dean Robert McNulty, D.D.S., is our honorary member and has given us his enthusiastic support by furnishing our tumor board room.

Oral cancer occurs in a wide variety of forms and in different degrees of malignancy. A flexible treatment program is therefore required, adaptable to each individual case. In some instances, cancer is best treated by operative methods, while in others it responds best to radium and roentgen-ray therapy alone, and, in still others, both surgery and radiation are required.

Cancers in the different parts of the oral cavity are somewhat similar in their histopathology but differ completely in their degree of malignancy, clinical course, mode of dissemination, treatment, and prognosis.

Early recognition of cancer determines in a high percentage of cases

whether therapy will be successful and the patient will survive. For this reason, it is necessary to investigate closely whenever a patient complains of a "vague feeling of something" in the mouth. Benign tumors, though they may seem ever so insignificant, are abnormal and may be in the process of changing toward the malignant under the influence of irritation.

Case 1

DR. FOWKES: The first patient for our lip symposium this morning is a woman, aged 32. She presented herself to the Dental Clinic with a history of frequent sores and crusts on the lower lip. Her history began as a teenager when she endeavored to decrease her hypersensitivity to sunshine by frequent overexposures, which resulted in a blistering of the mucous membranes of her lips as well as all exposed skin. During the past few years, a constant crusting has been present, and, more recently, when the crusts loosen and drop off, some bleeding occurs. Her past history suggests an individual who is abnormally sensitive to actinic radiation; a history of trauma or smoking is not given (Fig. 1).

The family history disclosed the fact that her mother has a similar skin and had numerous keratoses over the face and dorsum of the hands.

The examination discloses a woman with red hair and abnormal pigmentation over the forehead and prominences of the cheeks and neck from overexposure to sunlight. The lower lip is slightly swollen and the mucous membrane covering it is completely abnormal from scar tissue and crusts. A keratosis is present on the right lower lip measuring 2 cm. long. Its borders are irregular and the crust is thoroughly adherent to the mucosa. Other keratoses are plainly visible.

DR. SVOBODA: This patient was admitted to our surgical clinic, and from our examination we considered the large lesion as potentially malignant and performed a biopsy.

FIGURE 1

DR. BULLOCK: The microscopic study of this biopsy material disclosed a hyperkeratosis and marked inflammation but no evidence of cancer.

DR. HAZLET: This patient is a typical example of one with a hypersensitive skin and mucous membrane who is highly susceptible to any form of irritation; if overexposure is indulged in, the development of precancerous and cancerous changes occurs.

DR. COLLINS: In view of the report on the microscopic study and the significant history, I would be inclined to advise such measures as would offer the maximum long-range insurance. If protective ointments appeared to be producing satisfactory results, watchful waiting might be justified.

DR. HAMILTON: I wonder if this microscopic report describes the true nature of this lesion. Owing to the extensiveness of this lesion, I suggest that the entire lesion be removed for microscopic study.

DR. SHARP: This patient has had keratoses on her lower lip for at least a ten-year period, with increasing numbers and sizes of these lesions. It is not likely that ointments will be effective, and we must assume that all of the exposed mucous membrane on the lower lip is of a precancerous type. In order that the diagnosis be complete and the patient be rid of this hazard, I suggest that the vermilion portion of the mucous membrane of the lower lip be carefully excised for further microscopic study and that the lower lip be re-covered by freeing the lingual portion of the mucosa sufficiently to draw it forward and suture it to the cutaneous

FIGURE 2

margin. These cheiloplasties are very satisfactory in re-covering the lip with normal mucous membrane and without deformity.

DR. BULLOCK: Multiple tissue sections from such a specimen are very desirable in this case to rule out a possible carcinoma in situ. Ordinarily one can rely on biopsy material from the most suspicious area of a lesion on the lip.

Case 2

DR. FOWKES: The second patient is a man, 83 years of age. The present illness began eight years ago when he noticed for the first time a white patch developing on his lower lip. He voluntarily suggested that it was due to the constant pipe smoking for fifty years and the fact that he always carried his pipe on the left side. He stated that this whitened area gradually became more opaque; he consulted his general physician who informed him that it was not serious but that he should seek immediate attention if a nodule, an ulcer, or a change in contour should occur. During the past three months he has noticed a tonguelike projection extending medially from the plaque, which is gradually enlarging.

His family history was negative for similar oral lesions or cancer.

The examination discloses a man in good general condition for his age, with a deeply pigmented skin and numerous keratoses over the forehead and temple suggesting his occupation as a farmer. The vermilion mucosa of the lower lip is abnormal, with several keratoses and irregular small patches of leukoplakia. A large plaque of leukoplakia is present on the left side, measuring 1.5 cm. in diameter with at least a 1-mm. thickness of keratin. Extending from this medial border, is a tonguelike projection of the similar process that has as yet not developed into the extreme hyperkeratosis. The margins are definite and do not suggest signs of early cancerous change. A more diffuse leukoplakia is evident on the buccal surfaces and to a lesser degree over the dorsum of the tongue. The oral leukoplakia is stained from smoking (Fig. 2).

DR. SVOBODA: An excision with a millimeter or two margin of safety was performed on this lesion last week for diagnosis as well as cure.

DR. BULLOCK: The microscopic study of this lesion disclosed marked hyperkeratosis, acanthosis, and parakeratosis. Dyskeratosis was seen throughout the epithelium. The diagnosis was precancerous leukoplakia. The term "precancerous," as used here, implies only the possibility, not the inevitability, of malignant transformation. This lesion is one of those "abnormal states" that is often a precursor of cancer.

DR. LOTT: Leukoplakia is incited by irritation from one of many extraneous stimuli, and in this instance smoking is the primary factor, while on the gingival tissues it is most frequently denture irritation. We must assume that individuals who form leukoplakia have an abnormal type of mucous membrane to begin with because not all of us develop leukoplakia under identical circumstances. For this reason, patients who produce a leukoplakial response to irritation should be examined regularly for the remainder of their lives.

DR. HAMILTON: We must not only recognize a precancerous type of leukoplakia but realize that there are local-

ized forms as well as diffuse generalized types throughout the oral cavity, and treatment must invariably depend on the microscopic diagnosis and extent of the process.

DR. SHARP: Localized, advanced leukoplakial lesions of this type on any of the oral surfaces should be excised rather than destroyed by cautery, electrodesiccation, or acid. The excision results in a linear, minimal scar rather than a large area of scar tissue that is just as vulnerable to irritation as the condition originally treated.

DR. HAZLET: Several types of trauma enter into this type of "pipe smoker's" lesion. Thermal and dehydration injury from the heat of the pipe stem, mechanical injury from the rough texture that tooth abrasion produces on the pipe stem, and, of considerable importance, the damaging effect of constant bathing of the tissue with salivary secretions containing tobacco products. This patient should be urged at least to give up the constant holding of the pipe in the mouth, if not to give up the use of tobacco altogether.

Case 3

DR. FOWKES: The third patient is a 37-year-old man who gives a history of cutting his upper lip with a razor two months previously. The scar was reopened twice with the razor during this interval, and it was not until three weeks previously that he first felt a small nodule in the wound. The past history was given of a hypersensitivity of the skin and mucosa of the lower lip to actinic radiation. During the past few years, keratoses have developed that drop off from time to time, but recently several have been present continuously.

The family history was irrelevant.

The examination discloses a nodule, 5 mm. in diameter, on the skin of the upper lip just above the mucocutaneous border. It is ulcerated in the center and appears to be craterlike in shape with a characteristic pearly, rolled margin. The lower margin extends down to and

FIGURE 3

invades the mucocutaneous margin. It is nontender and indurated on palpation (Fig. 3).

DR. STRAUB: From the short history, the classical crateriform shape of the lesion, and the induration, we must assume that this is a primary carcinoma of the skin of the upper lip that is invading the mucocutaneous border. This patient illustrates the rare instance in which skin carcinoma may invade mucous membrane. In more advanced cases, it is oftentimes impossible to determine whether the primary growth arose on the skin or on the mucous membrane. From the point of view of prognosis, it is most important to determine the site, since the cutaneous carcinomas have a much higher curability on the upper lip.

DR. BULLOCK: The site of origin, that is, whether skin or mucous membrane, cannot always be established by microscopic study. However, unless the lesion is confined to the vermilion border, clinical correlation is necessary to establish the fact that it began on the skin and extended onto the mucous membrane or vice versa.

DR. HAMILTON: The treatment of

FIGURE 4

this lesion should be the same as of most cutaneous carcinomas, namely, excision. This lesion might well be treated according to our plan of excision for biopsy and cure, since there is very little doubt about the character of the growth. By means of a vertical elliptical incision, this lesion can be removed and the wound closed by plastic repair so that there will be little or no deformity. The specimen may be cut transversely in preparation for microscopic study, and one can determine the margin of safety on the skin surface as well as at depth.

DR. HAZLET: Undoubtedly microscopic study of the surgical specimen will confirm the clinical diagnosis of carcinoma. For this patient, protection of the damaged mucosa of the lower lip is also going to be of extreme importance. He has demonstrated ability to produce malignant changes apparently in response to climatic irritation and he must now be carefully instructed in all possible means of protection for the future.

Case 4

DR. FOWKES: The fourth case is a white man, aged 57, who presents a history of a lesion on the lower lip of six months' duration. He smokes from one to two packages of cigarettes a day and has always had trouble with cigarette paper sticking to his lower lip, and it was on one of these occasions, when the mucous membrane was torn away with the cigarette paper, that the lesion started. During the interval, it has increased to its present size without symptoms. Past history of constant irritation and injury from smoking and overexposure to sunshine is given.

Examination discloses a completely abnormal mucous membrane covering the lower lip with many scars and irritative areas. On the left side of the lower lip, a superficial ulceration is present, 1 cm. in diameter on the vermilion surface, that extends from the mucocutaneous border posteriorly. The ulcerating surface has a fine granular appearance and is slightly depressed, which gives it a crater-like shape. The margins are only slightly rolled and show but little invasion. The lesion is indurated on palpation, and invasion would not be considered to be more than 3 mm. in depth. Lymph nodes were not palpable in the neck (Fig. 4).

DR. SVOBODA: A biopsy was taken of the posterior margin of this lesion last week. Dr. Bullock described the specimen as a squamous-cell carcinoma, Grade I plus.

DR. HAZLET: The mucous membranes on the upper and lower lip are dry and scarred and yet have a thin atrophic appearance. The atrophic changes are also present on the intraoral surfaces, and he has had a dry throat for many years. This patient illustrates the common observation that oral carcinoma never arises on a normal mucous membrane.

DR. SHARP: This lesion is ideally adaptable to treatment by surface radium. A plaquelike mold of proper dimensions may be applied to the surface of this growth and held in place by a U-shaped lead sheath. If the lead piece is 1 mm. thick, it can be fitted over the plaque and pressed gently against the lip on both sides below and held firmly in place. The dose of radiation should be calculated for the delivery of 6000 gamma roentgens at a depth of 3 mm. Radiation in this form will give a temporary reaction and finally result in a healthy, normal scar. This patient will be kept under regular systematic observation, and, if cervical adenopathy develops, a prompt suprahyoid neck

dissection will be performed. Prophylactic neck dissections are not recommended, since only one out of eighteen or twenty patients with carcinoma of the lip develops cervical adenopathy subsequent to destruction of the primary lesion.

Case 5

DR. FOWKES: The fifth case is a 62-year-old white man who had a lesion of the lower lip for a year and a half. At the onset he said that it looked like a canker sore and that he believed it was probably due to his habit of smoking two and three packages of cigarettes a day. At first it grew slowly, but during the last three months it has more than doubled in size, and for the first time he is experiencing an aching pain in his jaw. The past history is irrelevant except for the habit of smoking and that he has been edentulous for eight years.

The examination discloses an ulcerated, invasive growth involving the left half of the lower lip. The bulk of the ulceration is over the cutaneous surface, but it extends over the vermilion surface and down on the lingual surface of the lip and approximately 2 cm. beyond all margins of the ulceration. The growth is firmly adherent to the mandible and clinically invades it. Actually, this growth extends from the mid-line of the lower lip laterally for a distance of 5 cm., with involvement of the anterior 25 per cent of the tissues of the cheek. In the left side of the neck, the facial lymph node measures 1.5 cm. in diameter; a node in the left submaxillary triangle is the same size, another in the left upper carotid triangle is 2 cm. in diameter, and all must be considered metastatic (Fig. 5).

A left lateral oblique roentgenogram demonstrates an invasive, bone-destructive lesion infiltrating the alveolar ridge and the body of the mandible in the bicuspid area.

DR. FOGEL: A biopsy was taken from the ulcerated portion of the growth, and it proved to be a squamous-cell carcinoma, Grade II plus. On the basis of the evidence given, we believe that this growth has invaded the mandible and that the palpable nodes in the left submaxillary and carotid triangles are metastases.

FIGURE 5

DR. BULLOCK: This growth undoubtedly arose on the vermilion surface of the lower lip rather than from the cutaneous surface because of its rapid growth and relatively early cervical node involvement. It may be one of those more aggressive growths that arise in the mucocutaneous margin, which are considered more aggressive than growths primary on mucous membrane or skin alone. Undoubtedly, more nodes are involved in the left neck than are palpable, and consideration of a complete left radical neck dissection should be imperative.

DR. HAMILTON: Fortunately, this type of case is becoming increasingly rare, namely, an obviously aggressive growth in an advanced stage of development. Certainly the most radical surgery will be the only form of treatment that will offer the patient any satisfactory prognosis. Neglect as demonstrated by this patient is the circumstance that prevents a 100 per cent prognosis for cancer of the lip.

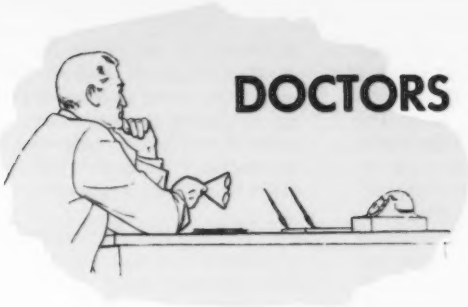
DR. SHARP: Widespread disease as described can only be treated by the most radical surgery without regard to ideal immediate reconstructive repair. A block resection of two thirds of the lower lip, the anterior third of the left cheek, the entire left mandible, and of

all of the contents of the left neck should be proposed for the treatment. With the extensive infiltrating primary lesion and the numerous metastases, no thought should be given to preservation of the angle and ascending ramus of the mandible for an immediate or delayed bone graft to reconstruct the mandibular arch.

DR. LOTT: In the past we have removed sections of the mandible and replaced the area with an immediate bone graft and other times have held the bone ends in normal approximation with vitallium plates temporarily until bone grafts could be fitted in the defect.

DR. FOGEL: As I recall, in all of those instances the primary lesions were small and with a single-node metastasis or none. In this case it seems to me that with the extensive removal of the portion of the left cheek, it would be impossible to perform a good approximation of the oral mucous membranes and a repair of the cheek and commissure of the lip and at the same time maintain the mandibular arch artificially or by actual bone graft. In my opinion this patient needs the most radical surgery without thought of a reconstruction of the mandible, which might increase the risk of local recurrence.

Probably the most mismanaged disease is inoperable and/or incurable malignancy. . . . Too often the patient is put in the care of the roentgenologist, and the family physician feels he has fulfilled his obligations. He is apt to inform the family there is nothing more he can do, and to see the patient as infrequently as possible, acting merely as the dispenser of narcotics. Thus go on months of torture and feeling of futility for the family as well as the patient. This tragically leads too frequently to quests for cure or relief from unethical practitioners. . . . There is nothing much more tragic than a dying cancer patient being shipped unnecessarily from one city to another, looking for the "cure." However, unless it is certain that the therapy is obviously a dishonest or useless procedure, the physician should not be too violent in objecting, if all proven palliative procedures have been of no avail. Finally the aid of the family pastor is often of greater benefit than psychotherapy or further palliative procedures any physician can offer. . . . A clever pastor by patience and repeated contact may open the mind of the sufferer to religious experiences that will bring a purposefulness to his pain and thereby make it bearable.—Taylor, S. G., III., and Slaughter, D.: The physician and the cancer patient. J.A.M.A. 150:1012, Nov. 8, 1952.



DOCTORS DILEMMAS

During the past year I have given several lectures to the public on various health topics. In the question period that follows, discussion of cancer and heart disease are the most intriguing topics. I have been asked repeatedly why the incidence of cancer mortality, as reported, is highest where deaths from vascular diseases are most frequent and lowest where vascular death rates are low. I have explained the seeming relationship as coincidental. Is there more documentation for this?

A The noted high incidence of cancer that exists along with high incidence of vascular disease can be attributed, in the main, to the greater longevity of populations in which they occur frequently. In this sense only, cancer may be called a disease of civilization. That is, as the death rates from infectious diseases, plagues, epidemics, etc., are reduced and childhood diseases are controlled, more of the population lives on beyond middle age and succumbs finally to the two disease groups that remain unchecked—cancer and heart disease. Obviously, the relationship between the two is apparent rather than real.

My patient is a 67-year-old white woman who was severely burned thirty-five years ago, with subsequent extensive scarring of the right forearm. One month ago this scar became ulcerated and was excised, followed by skin grafting. Sections of this tissue showed squamous-cell carcinoma, Grade I. This patient has just developed a mass on the inner surface of the arm, just below the elbow, which proved to be squamous-cell carcinoma involving the muscles. I should appreciate very much your opinion regarding further treatment.

A The recurrence of squamous carcinoma in a burn scar following apparently adequate excision is ominous. Providing there is no lymph-node involvement, however, excision of the recurrent tumor with wide margins may control the disease. It would be wise to inform the family that further recurrence of disease is a distinct possibility, in which instance amputation, possibly interscapulothoracic amputation, will be necessary.

One of our technicians was operated on eight months ago for a melanoma. Roentgenograms of the chest now show metastases. We should appreciate any information you might give us about new biological and chemical therapeutic agents used in the United States in this kind of cancer.

A There is little, of course, that can be expected from any form of therapy if there is proved metastasis to the lungs from melanoma. However, it has been reported that clinical regression of melanoma has followed treatment with antirabies serum, although the response

to this therapy in any significant number of patients has been disappointing. Treatment with thyroid hormone has also been associated, in a very few cases, with temporary regression of disease. More recently, it has been reported that TEPA (triethylenephosphoramide) has restrained the growth of transplanted melanoma in experimental animals, and in at least one human patient the drug was apparently responsible for dramatic, though temporary, regression of widespread tumors.

Q *Recently I have had a distressing problem. A 38-year-old housewife has become aware of her diagnosis of Hodgkin's disease. She is an avid reader of women's magazines and "medical reports" in the popular press and has come to me with the information that certain authorities have stated that Hodgkin's disease may be due to an infection. The patient is most concerned about the possibility of transmitting the disease to her three small children. I have told her that there was no evidence whatever to substantiate the statement that the disease is due to an infectious agent and that, more important, authorities who have treated many patients with Hodgkin's disease have failed to report any increased incidence of the disease in persons who have been in close contact, over long periods of time, with these patients.*

A Almost all authorities would agree with you. There is, indeed, little evidence that Hodgkin's disease is contagious in the usual sense. The speculations supporting a virus etiology of this disease are intriguing, but to date remain unproved.

Q *I have been treating a patient with ulcerative colitis for eleven years. He remains relatively under control, but his last two barium enemas, done at four-month intervals, show evidence of extensive multiple polyposis or "pseudopolyposis" of the colon. Although he continues almost entirely asymptomatic, this recent finding has prompted me to discuss the possibility of colectomy. Am I right in presuming that the roentgen-ray evidence justifies consideration of such a procedure?*

A Yes. Between 10 and 20 per cent of patients with multiple polyps of the colon develop cancer and 4 to 12 per cent of those with longstanding ulcerative colitis. With intelligent and sympathetic preparation for surgery, these patients frequently make remarkably successful adjustments and are able to appreciate the serious hazards that have been eliminated by the colectomy.

Q *How great is the reported increase in the incidence of lung cancer in men during recent years. I have been asked to talk on this subject to a fraternal group.*

A It is the most rapidly increasing form of cancer and may have already exceeded cancer of the stomach as the leading cause of cancer deaths in men. In 1949 cancer of the lung killed five times as many persons in the United States (16,660) as in 1933. You might be interested in showing a new film "The Warning Shadow" that was prepared for just such audiences by the American Cancer Society and the National Cancer Institute. It may be obtained through the American Cancer Society office in your State. In outline, the film tells the story of the first pneumonectomy for cancer of the lung (1933) and makes the point that early diagnosis and prompt treatment offer the possibility for cure. The original patient (still a practicing physician) and a number of other cured patients are shown at home and engaging in various pursuits. The film is nontechnical but explains clearly the reasons why early diagnosis is necessary if cancer is to be found before it has invaded other body sites.

new developments in cancer

Periodic Metabolic Examinations . . .

Casimir Funk, who in 1911 isolated the antiberiberi factor from rice polishings and invented the word VITAMIN to describe it, recently stated at the dedication of his new research laboratory in New York that periodic physical examinations of the future will include appropriate metabolic tests to reveal faulty blood chemistry that may be the basis of cancer and of many other diseases.

Cesium^{137} in Cancer . . .

Hodges and Lampe (Univ. Mich.) are comparing cesium^{137} with cobalt^{60} and conventional roentgen-ray therapy of cancer. Radioactive cesium has been separated from other radioactive substances produced in the pile at Oak Ridge. To date only limited amounts are available. Cesium^{137} may prove to be a valuable contribution to the radiation therapy of cancer. It is a high-powered, long-lived source of radiation.

Hidden Estrogen Source . . .

Huggins (Univ. Chicago) reports continuing excretion of female hormone in certain women after total adrenalectomy and ovariectomy and reasons that therefore, somewhere in the female body, there is a secret source of estrogen. Such patients naturally do not respond to conventional hormone treatment for cancer. If this cryptic source of estrogen can be located, it may be possible to increase the number of cancer patients responding to combined adrenalectomy and ovariectomy.

Hemostasis in Cancer . . .

Tamblyn (Lansing, Mich.) reports that hemorrhage in cancer, fibroid uterine tumor, threatened abortion, and other conditions can be controlled promptly by administration of antihemophilic globulin, a by-product of whole blood.

Rescue on the Table . . .

One of the great risks in radical surgery is shock. When the eosinophil count continues to rise and the blood pressure continues to fall despite copious transfusions and pressor agents, the patient is in real trouble. Hayes (Yale) has found that if, at this critical moment, the patient is treated with cortisone and bovine adrenocortical extract, both pressure and eosinophil levels return rapidly to normal. Cortisone alone acts too slowly to be of use. The tech-

nique has been used to rescue several patients from surgical shock and was successful in each instance.

Radar Therapy . . .

Rutgers investigators have been treating experimental cancers with radar. They implanted rats with carcinomas, which were allowed to grow from ten to fourteen days. Then, carefully matching current to tumor size and depth, the oscillator sent waves into the cancers. Treatment periods varied from twenty seconds to three minutes. From twenty-four to seventy-two hours later the tumors darkened, opened, and drained and scabs sloughed off later. Healing was completed from three weeks to a month later. Of the 136 animals treated, 100 (or 74 per cent) were completely cured. Of these, 36 per cent showed immune resistance to further transplants. One drawback is that normal tissue is as susceptible to the radar waves as is tumor. The technique now is being applied to a few dog tumors.

Methylcholanthrene Therapy . . .

Kinosita (UCLA), who last year secured complete regressions in 100 per cent of animals treated with TEM, this year is achieving similar remissions with the standard laboratory carcinogen, methylcholanthrene. The rats usually die on the seventh or eighth day after inoculation with ascites tumor—probably the most malignant of all experimental tumors. Kinosita treats them on the third or fourth day. Treated animals are showing cell changes—the formation of "orphan nuclei"—indicative of regression about the time the untreated animals start to die. He now is following the chemical changes involved in regression.

Longevity of Hodgkin's Patients . . .

One of the controversies in cancer chemotherapy revolves around the contention that some agents, besides bringing frequent subjective and sometimes objective relief, extend the life expectancy of patients. This is a tough point to prove. Lacking controls in human experiments, the only standard of measurement is the doctor's best guess based upon his experience. Rottino and others (St. Vincent's) have started long-term observations on the effect of nitrogen mustard and TEM. The study, which will take five years to complete, may give an answer so far as Hodgkin's disease patients are concerned.

Cholesterol Conditions . . .

Scientists on both coasts discovered independently a few months ago that cholesterol is synthesized by cell-free tissue minces as well as by cells. Greenberg (Cal.) noted that when he added acetate to a liver mince he produced substantial quantities of cholesterol. A few intact red cells were in the mince. A short time later, Bucher (Mass. General) used rat-liver mince as a control to compare its performance with that of suspended liver cells. She was amazed to find that the cell-free mince synthesized more cholesterol than intact cells. The discoveries have inspired intensive study. It is possible that a method for cholesterol synthesis may be perfected and the diseases dependent upon cholesterol (including a host of heart and circulatory conditions) can be controlled.

Hodgkin's Disease and Diet . . .

Ohio State investigators have maintained eight Hodgkin's patients for from two to six weeks on protein-free diets containing the essential amino acids. They found that the patients' amino acid requirements were normal. The patients suffered severe anorexia, fatigue, and mental depression when deprived of required amounts of amino acids. No conclusions were reached on the effects of the diet on their disease.

COMING MEDICAL MEETINGS

Date	Association	City	Place
1953			
July 20-22	Postgraduate Medical Assembly South Texas	Houston	Shamrock
Aug. 10-14	National Medical Association	Nashville	Meharry Medical College
Aug. 24-29	World Conference on Medical Education	London	British Medical Assoc. House
Aug. 31-Sept. 3	American Hospital Association	San Francisco	Convention Hall
Aug. 31-Sept. 6	World Medical Association	Amsterdam	
Sept. 6-12	6th International Congress of Microbiology	Rome	
Sept. 9-12	Rocky Mountain Medical Conference	Salt Lake City	
Sept. 12-16	Washington State Medical Association	Seattle	Olympic
Sept. 14-17	International College of Surgeons	New York	Waldorf-Astoria
Sept. 15-20	Congress of the International Society of Surgery	Lisbon, Portugal	
Sept. 20-24	Pennsylvania State Medical Society	Pittsburgh	William Penn
Sept. 22-24	Kentucky State Medical Association	Louisville	Columbia Auditorium
Sept. 23-25	Michigan State Medical Society	Grand Rapids	Auditorium
Sept. 28-Oct. 1	American Dental Association	Cleveland	Auditorium
Sept. 29-Oct. 2	American Roentgen Ray Society	Cincinnati	Netherland Plaza
Oct. 5-9	American College of Surgeons	Chicago	Conrad Hilton
Oct. 11-17	National Gastroenterological Association	San Francisco	Biltmore
Oct. 12-16	American Society of Clinical Pathologists	Chicago	Drake
Oct. 25-27	California Academy of General Practice	Coronado	Hotel del Coronado
Nov. 2-6	American Cancer Society Annual Meeting	New York	Hotel Commodore
Nov. 3-4	American Cancer Society Scientific Session: Cancer of the Lung	New York	Hotel Commodore

Printed in U.S.A.

Is It Cancer?

For nearly a century the answer to this question has been obtainable from the biopsy.

May 15, 1887—Crown Prince Frederick of Prussia: "Is it cancer?" Morrell Mackenzie: "No!" This answer was strengthened by the report of Rudolf Virchow, founder of cellular pathology in 1858, on the three bits of the tumor given him by Mackenzie.

November 6, 1887—Crown Prince Frederick: "Is it cancer?" Sir Morrell Mackenzie (knighted by Queen Victoria, September 7): "I am sorry to say, Sir, it looks very much like it but it is impossible to be certain." Removal of larynx, recommended in consultation, was refused.

February 8, 1888—Death by suffocation averted by tracheotomy.

June 15, 1888—Death with copious discharge of pus from tracheotomy tube and signs of terminal pneumonia. Autopsy by Virchow: Characteristic carcinoma of larynx; metastasis to lymph nodes. Numerous abscesses in lower lobes of the lungs. Virchow emphasized the importance of obtaining representative tissue for biopsy. Mackenzie in "The Fatal Illness of Frederick the Noble" maintained that the tumor became malignant after his first examination and blamed the treatment given by the German physicians, for which imprudence he was censured by the Royal College of Surgeons.

During the terminal stages of Frederick's illness, Mackenzie was in cable communication with Dr. George F. Shrady, one of the consulting surgeons of General Ulysses S. Grant who died of a similar ailment three years before.

August, 1884—General Grant complained of sore throat and tenderness in the roof of the mouth and was treated for chronic throat affection for some months. Surgical consultation then revealed malignant tumor and operation was considered inadvisable.

May 6, 1885—Letter from Dr. Fordyce Barker, Grant's family physician, to Dr. John Rogers: "Gen'l Grant has epithelioma, involving left tonsil, uvula, pharynx, base of the tongue and enlargement of right cervical glands. . . . I think it possible that he will live until next winter unless new casualties occur which break down his general system. . . . The microscopic evidence seems conclusive that the disease is epithelioma and that nothing in the clinical history is opposed to this theory. All the medical attendants have been in entire agreement as to the nature of the case and the appropriate treatment."

July 23, 1885—General Grant died.

Is it cancer?—The question asked by General Grant, by Prince Frederick, by Grover Cleveland, by Napoleon, and by millions of others is being asked more and more often with the spread of knowledge concerning the early signs of cancer.

The pathologist finds the answer in the biopsy.